Low- and high-LET radiation drives clonal expansion of lung progenitor cells in vivo.

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Public Summary:
Abundant populations of epithelial progenitor cells maintain the epithelium along the proximal-to-distal axis of the airway. Exposure of lung tissue to ionizing radiation leads to tissue remodeling and potential cancer initiation or progression. In this study we determined how lung epithelial progenitor cells respond to different doses and energy levels of ionizing radiation. We found that radiation markedly reduces lung progenitor cell function in a dose and energy-dependent fashion. Consistent with this finding we were able to show that remaining progenitor cells underwent significantly more clonal expansion for epithelial maintenance. This work provides novel insights into the effects of ionizing radiation exposure on airway epithelial progenitor cell behavior.

Scientific Abstract:
Abundant populations of epithelial progenitor cells maintain the epithelium along the proximal-to-distal axis of the airway. Exposure of lung tissue to ionizing radiation leads to tissue remodeling and potential cancer initiation or progression. However, little is known about the effects of ionizing radiation on airway epithelial progenitor cells. We hypothesized that ionizing radiation exposure will alter the behavior of airway epithelial progenitor cells in a radiation dose- and quality-dependent manner. To address this hypothesis, we cultured primary airway epithelial cells isolated from mice exposed to various doses of 320 kVp X ray or 600 MeV/nucleon (56)Fe ions in a 3D epithelial-fibroblast co-culture system. Colony-forming efficiency of the airway epithelial progenitor cells was assessed at culture day 14. In vivo clonogenic and proliferative potentials of airway epithelial progenitor cells were measured after exposure to ionizing radiation by lineage tracing and IdU incorporation. Exposure to both X rays and (56)Fe resulted in a dose-dependent decrease in the ability of epithelial progenitors to form colonies in vitro. In vivo evidence for increased clonogenic expansion of epithelial progenitors was observed after exposure to both X rays and (56)Fe. Interestingly, we found no significant increase in the epithelial proliferative index, indicating that ionizing radiation does not promote increased turnover of the airway epithelium. Therefore, we propose a model in which radiation induces a dose-dependent decrease in the pool of available progenitor cells, leaving fewer progenitors able to maintain the airway long-term. This work provides novel insights into the effects of ionizing radiation exposure on airway epithelial progenitor cell behavior.